Review

Electrocardiogram ST Analysis During Labor

A Systematic Review and Meta-analysis of Randomized Controlled Trials

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OBJECTIVE: To compare the effectiveness of cardiotocography plus ST analysis with cardiotocography alone during labor.

DATA SOURCES: Randomized controlled trials were identified by searching electronic databases.

METHODS OF STUDY SELECTION: We included all randomized controlled trials comparing intrapartum fetal monitoring with cardiotocography plus ST analysis with cardiotocography alone. The primary outcome (ie, perinatal composite outcome) was a composite of intrapartum fetal death, neonatal death, Apgar score 3 or less at 5 minutes, neonatal seizure, metabolic acidosis (defined as umbilical arterial pH 7.05 or less, and extracellular fluid base deficit 12 mmol/L or greater), intubation for ventilation at delivery, or neonatal encephalopathy.

TABULATION, INTEGRATION, AND RESULTS: Six randomized controlled trials, which included 26,529 laboring singletons with cephalic presentation at term, were analyzed. Compared with women who were randomized to cardiotocography, those who were randomized to ST analysis and cardiotocography had a similar incidence of perinatal composite outcome (1.5% compared with 1.6%; relative risk [RR] 0.90, 95% confidence interval [CI] 0.74–1.10; five studies), neonatal metabolic acidosis (0.5% compared with 0.7%; RR 0.74, 95% CI 0.54–1.02; five studies), admission to the neonatal intensive care unit (5.4% compared with 5.5%; RR 0.99, 95% CI 0.90–1.10; six studies), perinatal death (0.1% compared with 0.1%; RR 1.71, 95% CI 0.67–4.33; six studies), neonatal encephalopathy (0.1% compared with 0.2%; RR 0.62, 95% CI 0.25–1.52; six studies), cesarean delivery (13.8% compared with 14.0%; RR 0.96, 95% CI 0.85–1.08; six studies), and operative delivery (either cesarean or operative vaginal delivery) (23.9% compared with 25.1%; RR 0.93, 95% CI 0.86–1.01; six studies).

CONCLUSION: The use of ST analysis during labor as an adjunct to the standard cardiotocography does not improve perinatal outcomes or decrease cesarean delivery.

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Fetal metabolic acidosis is one of the essential criteria to define an intrapartum hypoxic event according to the American College of Obstetricians and Gynecologists.[1] It is associated with several short- and long-term neonatal complications, including cerebral palsy and death.[2,3]

Cardiotocography has been developed as a form of continuous electronic fetal monitoring of heart rate with the aim of detecting fetal hypoxia during labor and hence preventing metabolic acidosis. Despite being the standard for intrapartum management in the United States, this technique, as a result of its high false-positive rate, significantly increases the cesarean and operative vaginal delivery rate and is associated only with less seizures as neonatal benefit, whereas perinatal mortality is not affected.[4,5] Moreover, the evaluation of cardiotocography is associated with high

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intra- and interobserver variability.[4,6] Given these shortcomings of cardiotocography, research has focused on alternatives, or at least techniques that could decrease the false-positive rate of electronic fetal monitoring, and improve neonatal outcomes such as metabolic acidosis and death. Fetal ST waveform analysis, based on electrocardiogram changes determined by the myocardial adaptation to oxygen deficiency, has been studied combined with cardiotocography in several randomized trials in the hope to decrease cesarean delivery rates with contradictory results regarding its ability to improve cardiotocography effectiveness.[7–12]

The purpose of this meta-analysis was to compare the effectiveness of cardiotocography alone or with additional ST waveform analysis monitoring during labor to lower the rate of adverse neonatal outcome.

SOURCES

The review protocol was established by two investigators (G.S., V.B.) before commencement and was registered with the PROSPERO International Prospective Register of Systematic Reviews (registration No. CRD42015019421).

Two authors (G.S., V.B.) identified trials by searching independently the electronic databases MEDLINE, Scopus, ClinicalTrials.gov, the PROSPERO International Prospective Register of Systematic Reviews, EMBASE, and the Cochrane Central Register of Controlled Trials with the use of a combination of text words: "ST analysis," "STAN," "cardiotocography," "intrapartum fetal monitoring," "CTG," "randomized trial," "metabolic acidosis," "EFM," "electrocardiogram," and "labor" from inception of each databases until August 2015.

STUDY SELECTION

We included all randomized controlled trials (RCTs) comparing intrapartum electronic fetal monitoring with cardiotocography plus ST waveform analysis (STAN group) compared with cardiotocography alone (control group). Selection included singleton gestations in cephalic presentation at term or near term in labor. Randomized trials using PR interval and not ST waveform analysis were excluded. Studies in multiple gestations and quasirandomized trials (ie, trials in which allocation was done on the basis of a pseudorandom sequence, for example, odd–even hospital number or date of birth, alternation) were also excluded.

The risk of bias in each included study was assessed by using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions.[13] Seven domains related to risk of bias were assessed in each included trial because there is evidence that these issues are associated with biased estimates of treatment effect: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcome assessment; 5) incomplete outcome data; 6) selective reporting; and 7) other bias. Review authors' judgments were categorized as "low risk," "high risk," or "unclear risk" of bias.[13]

Two authors (G.S., V.B.) independently assessed inclusion criteria, risk of bias, and data extraction. Disagreements were resolved by consensus through discussion. Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. Differences were reviewed and further resolved by common review of the entire process. Data not presented in the original publications were requested from the principal investigators.

Primary and secondary outcomes were defined before data extraction. The primary outcome was perinatal composite outcome, defined as at least one of the following: intrapartum fetal death, neonatal death, Apgar score 3 or less at 5 minutes, neonatal seizure, metabolic acidosis (defined as umbilical arterial pH 7.05 or less and extracellular fluid base deficit 12 mmol/L or greater), intubation for ventilation at delivery, or neonatal encephalopathy. Secondary outcomes included incidence of metabolic acidosis, admission to the neonatal intensive care unit, perinatal death (ie, either stillbirth or neonatal death), hypoxic–ischemic encephalopathy, meconium aspiration syndrome, shoulder dystocia, need for fetal blood sampling, and type of delivery. We planned to assess the primary outcome in sensitivity analyses according to the inclusion criteria of the trials and according to the ST waveform analysis method used.

The data analysis was completed independently by two authors (G.S., V.B.) using Review Manager 5.3.[13] The completed analyses were then compared, and any difference was resolved with review of the entire data and independent analysis. Statistical heterogeneity between studies was assessed using the Higgins I^2 statistic.[13] In case of statistically significant heterogeneity (I^2 50% or greater), the random effects model of DerSimonian and Laird was used to obtain the pooled risk estimate; otherwise, a fixed-effects model was utilized.[13] The summary measures were reported as relative risk (RR) with 95% confidence interval (CI) with an RR less than 1 indicating treatment benefit. $P<.05$ was considered statistically significant. Potential publication biases were assessed graphically by using a funnel plot and statistically by using Begg's and Egger's tests.[13]

The meta-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement.[14]

RESULTS

Six RCTs met inclusion criteria for this meta-analysis and were analyzed (Appendix 1, available online at http://links.lww.com/AOG/A738).[7–12] The overall risk of bias was low (Fig. 1). All the included studies had a low risk of bias in random sequence generation. Adequate methods for allocation of women were used in all six of the RCTs. Blinding was considered difficult methodologically given the intervention, and only one study used a masked ST waveform analysis fetal heart rate monitor to achieve blinding.[12] Blinding the assessors to the outcome was adequate in all trials. Appendix 2, available online at http://links.lww.com/AOG/A739, shows the funnel plot for the primary outcome for assessing publication bias; the symmetric plot suggests no publication bias. Publication bias, assessed using Begg's and Egger's tests, showed no significant bias ($P=.39$ and $P=.33$, respectively).

All studies enrolled only singleton gestations with cephalic presentation in active labor and excluded women with multiple pregnancy or with noncephalic position (Tables 1 and 2).[7–12] One trial was significantly different from the others regarding inclusion criteria: the French RCT included only women with abnormal cardiotocography in labor and excluded normal cardiotocography cases and cardiotocography with no decelerations.[10] The inclusion of women with pathologic cardiotocography at startup of the ST waveform analysis in the French RCT deviated from the ST waveform analysis clinical guidelines.[15] Three RCTs included high-risk cephalic singletons in labor who needed continuous cardiotocography (ie, high-risk pregnancy: pre-existing maternal disease, complicated obstetric history, hypertensive disorders, intrauterine growth restriction, ruptured membranes for more than 24 hours, postdate gestational age, failure to progress, need for pain relief, meconium-stained amniotic fluid, or nonreassuring fetal heart rate at intermittent auscultation by a midwife),[7,8,11] whereas the other two included all cephalic singletons in labor (ie, both high-risk and low-risk pregnancies).[9,12]

In all included studies all participating clinical care providers and research personnel were trained in the correct use of ST waveform analysis. One trial included a 100-case test period before enrollment[8]; the Swedish RCT required a 2-month practice period before enrollment started and there was retraining during the trial[7]; the Dutch RCT required certification and a 2-month practice period before enrollment started[11]; the American trial required a 50-case test period, four levels of training as well as three levels of certification[12]; the other two RCTs offered some form of pretrial training but the time was not reported.[9,10] An interim analysis was performed in all but two RCTs.[9,10]

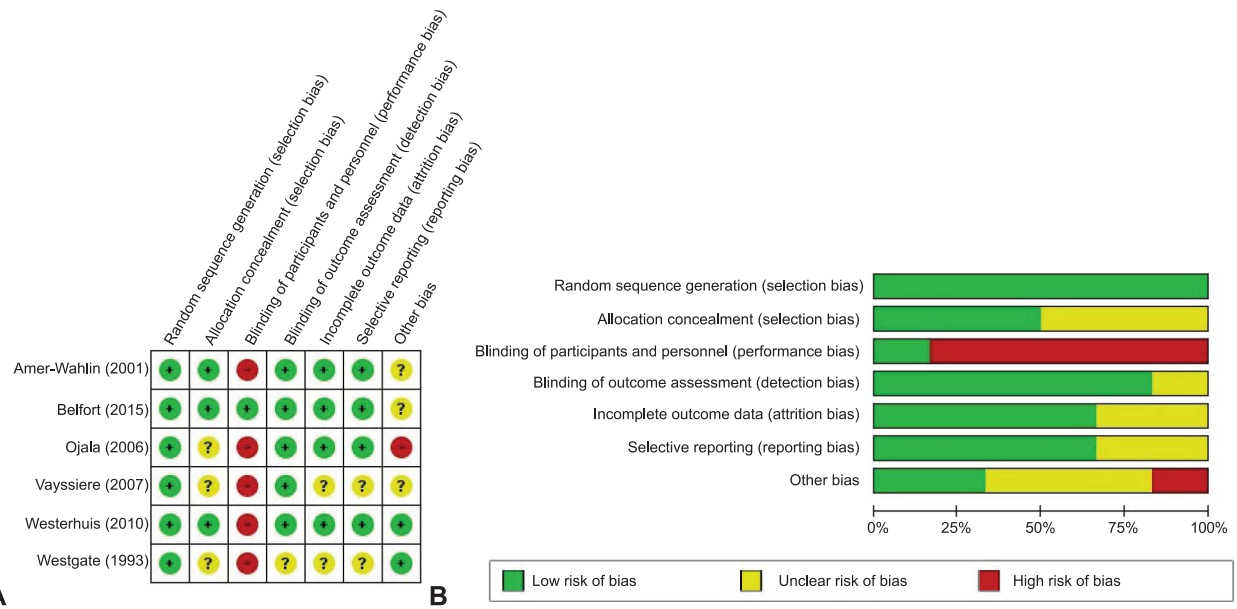

Fig. 1. Assessment of risk of bias. **A**. Summary of risk of bias for each trial. Plus sign, low risk of bias; minus sign, high risk of bias; question mark, unclear risk of bias. **B**. Risk of bias graph about each risk of bias item presented as percentages across all included studies.

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Table 1. Descriptive Data of the Included Trials

Reference	Study Location	No. of Patients at Randomization	Gestational Age at Randomization (wk)	Inclusion Criteria	Primary Outcome
Westgate et al,[8] 1993	England	2,434 (1,219/1,215)	Greater than 34	High-risk laboring women, singleton fetus, cephalic position	Operative deliveries
Amer-Wahlin et al,[7] 2001	Sweden	5,049 (2,565/2,484)	36 or greater	Laboring women, singleton fetus, cephalic position, continuous CTG needed*	Neonatal metabolic acidosis
Ojala et al,[9] 2006	Finland	1,472 (733/739)	36 or greater	Laboring women, singleton fetus, cephalic position	Umbilical artery pH less than 7.10
Vayssiere et al,[10] 2007	France	799 (399/400)	36 or greater	Laboring women, singleton fetus, cephalic position, abnormal CTG (or thick meconium in 7%)	Operative deliveries
Westerhuis et al,[11] 2010	The Netherlands	5,667 (2,827/2,840)	36 or greater	Laboring women, singleton fetus, cephalic position, continuous CTG needed*	Neonatal metabolic acidosis
Belfort et al,[12] 2015	United States	11,108 (5,532/5,576)	36 or greater	Laboring women, singleton fetus, cephalic position, cervical dilatation 2–7 cm	Composite neonatal outcome
Total	—	26,529 (13,275/13,254)	—	—	—

CTG, cardiotocography.
Data are total n (ST waveform analysis group/CTG only).
* Continuous CTG needed in pregnancies complicated by pre-existing maternal disease, complicated obstetric history, hypertensive disorders, intrauterine growth restriction, rupture membranes for more than 24 hours, a postdate gestational age, failure to progress, need for pain relief, meconium-stained amniotic fluid, or nonreassuring fetal heart rate at intermittent auscultation by a midwife.[7,11]

Protocols for management in both the cardiotocography and the STAN groups were well described and followed specific guidelines based on combined evaluation of cardiotocography and ST waveform analysis. The ST waveform analysis guideline involved categorization of the conventional fetal heart rate pattern into one of the three color-coded categories (ie, green zone, yellow zone, and red zone) (Appendix 3, available online at http://links.lww.com/AOG/A740).[15–17] The intended use of this fetal heart rate

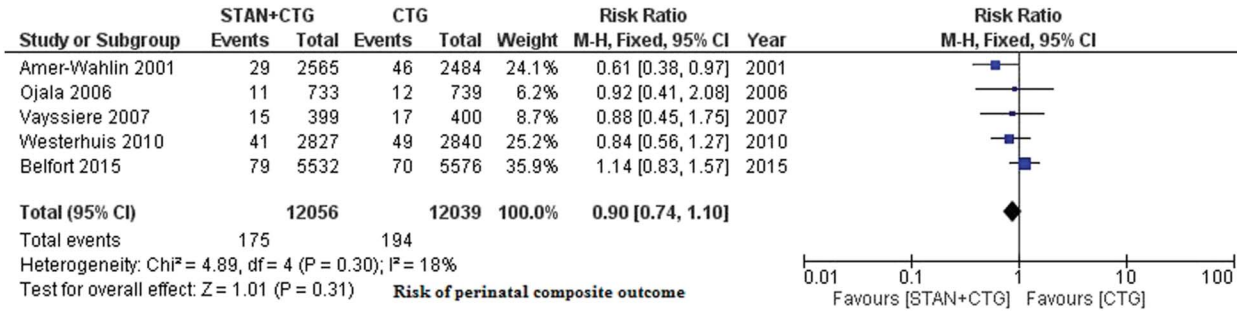

Fig. 2. Forest plot for the risk of the primary outcome (ie, perinatal composite outcome), that is, a composite of at least one of the following: intrapartum fetal death, neonatal death, Apgar score of 3 or less at 5 minutes, neonatal seizure, metabolic acidosis, intubation for ventilation at delivery, or neonatal encephalopathy. STAN, ST analysis; CTG, cardiotocography; M-H, Mantel-Haenszel; CI, confidence interval; df, degrees of freedom.

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Table 2. Characteristics of the Included Trials

Reference	No. of Centers	Months of Study	STAN Model Used	Prestudy Training	Interim Analysis	STAN Guidelines for Intervention
Westgate et al,[8] 1993	1	18	8801	Yes, with 100 cases	Yes, after 1,200 cases	4-tier system
Amer-Wahlin et al,[7] 2001	3	18	S21*	Yes, during 2 mo, certification of users	Yes, after 1,600 cases	4-tier system
Ojala et al,[9] 2006	1	14	S21*	Yes, but time not reported	No information	4-tier system
Vayssiere et al,[10] 2007	2	27	S21*	Yes, but time not reported	Not planned	4-tier system
Westerhuis et al,[11] 2010	9	30	S21 and S31*	Yes, at least 2 mo, certification of users	Serious events monitored by Safety Committee	4-tier system
Belfort et al,[12] 2015	26	48	S31*	Yes, during 7 mo, 50 cases, certification of users	Yes, but time not reported; serious events monitored by Safety Committee	3-tier system

STAN, ST analysis.
* STAN S21 and S31, automatic warning monitor.[7,9–12]

classification system is to suggest clinical conditions in which adjunctive use of ST waveform changes may aid the interpretation of specific fetal heart rate patterns. A difference between the European RCTs and the American RCT was that later in the use of this technology, the European changed the three-tier system for the STAN group to the four-tier system, whereas Belfort et al did not follow this system since the U.S. Food and Drug Administration had approved the three-tier systems. Therefore, four studies use the same protocol for ST waveform analysis (ie, four-tier system),[7,9–11] whereas in the American RCT, management was based on a three-tier system (Appendix 3, http://links.lww.com/AOG/A740).[17] In one study, the STAN 8801 recorder was used,[8] whereas the other studies used the STAN S21, S31, or both. The S21 and the S31 monitors provide an automatic assessment of the ST changes and give an automatic warning in case of significant changes (fetal information was displayed on a monitor and an alert was generated when the computer detected a concerning pattern), whereas in the 8801, the ST changes were identified by visual analysis. All the included studies explicitly reported an intention-to-treat analysis. Authors of one trial[7] have published a reanalysis of the study, including a correction of some errors in the original analysis. We used the most accurate and up-to-date data available for that trial. Only the American RCT reported data regarding the primary outcome. Four authors provided unpublished data from their original trials to obtain those regarding perinatal composite outcome (ie, primary outcome) and those regarding the incidence of metabolic acidosis according to the definition used in the American RCT (ie, umbilical arterial pH 7.05 or less and extracellular fluid base deficit 12 mmol/L or greater).[7,9–11]

Of the 26,529 women included in the meta-analysis, 13,275 were randomized to the STAN group (STAN+CTG) and 13,254 to the control group (CTG alone) (Table 1). The STAN group had a similar incidence of perinatal composite outcome: 1.5% compared with 1.6% (RR 0.90, 95% CI 0.74–1.10; Fig. 2; Appendix 3, http://links.lww.com/AOG/A740). The statistical heterogeneity between the studies was low ($I^2=18\%$).

Women who were randomized to the STAN group had a similar rate of neonatal metabolic acidosis (0.5% compared with 0.7%; RR 0.74, 95% CI 0.54–1.02 when defined as umbilical arterial pH 7.05 or less and extracellular fluid base deficit 12 mmol/L or greater; five studies included; 0.7% compared with 1.0%; RR 0.81, 95% CI 0.44–1.46 when defined as umbilical arterial pH less than 7.05 and extracellular fluid base deficit greater than 12 mmol/L; five studies included), admission to the neonatal intensive care unit (5.4% compared with 5.5%; RR 0.99, 95% CI 0.90–1.10; six studies), perinatal death (0.1% compared with 0.1%; RR 1.71, 95% CI 0.67–4.33; six studies), neonatal encephalopathy (0.1% compared with 0.2%; RR 0.62, 95% CI 0.25–1.52; six studies), meconium aspiration syndrome (0.4% compared with 0.3%; RR 1.01, 95% CI 0.54–1.87; one study), and shoulder dystocia (2.5% compared with 2.8%; RR 0.90, 95% CI 0.72–1.13; one study) (Appendix 3, http://links.lww.com/AOG/A740, and Appendix 4, available online at http://links.lww.com/AOG/A741). All included RCTs, except one in which this procedure was not used in either group,[12] reported the number of individuals who had fetal scalp blood samples taken but

no information was available regarding the number of times samples were taken from the same individual. In four studies, the indication for a fetal blood sample was described as optional or at a doctor's judgment.[7–10] In one trial, three indications for fetal blood samples were defined in the STAN group: abnormal cardiotocography at the start of a ST waveform analysis recording, tiny electrocardiographic signal (ie, poor electrocardiographic signal quality defined as absence of ST information for more than 4 minutes or less than one average electrocardiographic complex per minute), or more than 1 hour of abnormal cardiotocography without the ST waveform analysis.[11] For the control group the fetal blood samples were taken after a short period of abnormal tracing. The incidence of fetal blood sampling was significantly lower in the STAN group compared with the control group (8.3% compared with 17.2%; RR 0.59, 95% CI 0.45–0.79; five studies; Appendix 5, available online at http://links.lww.com/AOG/A742). Nevertheless, the statistical heterogeneity within the studies was high (I^2=91%) (Table 3). Regarding type of delivery, no significant difference was found in the incidence of cesarean delivery (13.8% compared with 14.0%; RR 0.96, 95% CI 0.85–1.08; six studies) or operative delivery (either cesarean delivery or operative vaginal delivery) (23.9% compared with 25.1%; RR 0.93, 95% CI 0.86–1.01; six studies), whereas the incidence of operative vaginal delivery (either forceps or vacuum) was significantly lower in the STAN group compared with the control group (10.1% compared with 11.1%; RR 0.91, 95% CI 0.85–0.98; six studies) (Table 4; Appendix 6, available online at http://links.lww.com/AOG/A743). The statistical heterogeneity within the RCTs was low (I^2 less than 50%) for most of the secondary outcomes (Tables 3 and 4). Appendix 7, available online at http://links.lww.com/AOG/A744, shows the funnel plot for the outcomes; the symmetric plots suggest no publication bias.

The STAN group had a similar incidence of the primary outcome (ie, perinatal composite outcome) compared with the control group in subgroup analysis of trials that used the automatic ST waveform analysis (ie, STAN S21, S31, or both) (RR 0.94, 95% CI 0.75–1.19),[7,9–12] in subgroup analysis of trials in which normal cardiotocography cases were not excluded (RR 0.92, 95% CI 0.75–1.14),[7,9,11,12] in subgroup analysis of trials in which women were randomized at 36 weeks of gestation or greater (RR 0.94, 95% CI 0.75–1.19),[7,9–12] in subgroup analysis of trials including only high-risk singleton gestations (RR 0.73, 95% CI 0.53–1.00),[7,11] in subgroup analysis of trials including all cephalic laboring singleton gestations (RR 1.14, 95% CI 0.85–1.53),[9,12] in

Table 3. Primary and Secondary Outcomes

Reference	Composite Perinatal Outcome	Neonatal Metabolic Acidosis*	Neonatal Metabolic Acidosis†	NICU
Westgate et al,[8] 1993	N/R	N/R	5/1,219 (0.4) vs 13/1,215 (1.1)	24/1,219 (2.0) vs 31/1,215 (2.6)
Amer-Wahlin et al,[7] 2001	29/2,565 (1.1) vs 46/2,484 (1.9)	25/2,565 (1.0) vs 38/2,484 (1.5)	12/2,519 (0.5) vs 24/2,447 (1.0)	132/2,519 (5.2) vs 151/2,447 (6.2)
Ojala et al,[9] 2006	11/733 (1.5) vs 12/739 (1.6)	6/733 (0.8) vs 4/739 (0.5)	12/714 (1.7) vs 5/722 (0.7)	26/714 (3.6) vs 26/722 (3.6)
Vayssiere et al,[10] 2007	15/399 (3.8) vs 17/400 (4.3)	11/399 (2.8) vs 9/400 (2.3)	8/399 (2.0) 5/400 (1.3)	5/399 (1.3) vs 6/400 (1.3)
Westerhuis et al,[11] 2010	41/2,827 (1.5) vs 49/2,840 (1.7)	20/2,827 (0.7) vs 28/2,840 (1.0)	20/2,827 (0.7) vs 30/2,840 (1.1)	40/2,827 (1.4) vs 45/2,840 (1.6)
Belfort et al,[12] 2015	79/5,532 (1.4) vs 70/5,576 (1.3)	3/5,532 (0.1) vs 8/5,576 (0.1)	N/R	498/5,532 (9.0) vs 470/5,576 (8.4)
Total	175/12,056 (1.5) vs 194/12,039 (1.6)	65/12,056 (0.5) vs 87/12,039 (0.7)	57/7,678 (0.7) vs 77/7,624 (1.0)	725/13,210 (5.4) vs 729/13,200 (5.5)
I^2 (%)	18	0	60	0
Method used	M-H, fixed	M-H, fixed	M-H, random	M-H, fixed
RR (95% CI)	0.90 (0.74–1.10)	0.74 (0.54–1.02)	0.81 (0.44–1.46)	0.99 (0.90–1.10)

NICU, admission to neonatal intensive care unit; N/R, not reported; N/P, not performed; N/A, not applicable; M-H, Mantel-Haenszel test; RR, relative risk; CI, confidence interval.

Data are n ST waveform analysis group vs n cardiotocography-only group with percentage unless otherwise sepecified.

Composite perinatal outcome, a composite of at least one of: intrapartum fetal death, neonatal death, Apgar score 3 or less at 5 minutes, neonatal seizure, metabolic acidosis (ie, umbilical arterial pH 7.05 or less and extracellular fluid base deficit 12 mmol/L or greater), intubation for ventilation at delivery, or neonatal encephalopathy.

Bold indicates statistical significance.

* Neonatal metabolic acidosis defined as umbilical arterial pH 7.05 or less and extracellular fluid base deficit 12 mmol/L or greater.

† Neonatal metabolic acidosis defined as umbilical arterial pH less than 7.05 and extracellular fluid base deficit greater than 12 mmol/L.

subgroup analysis of trials that enrolled only abnormal cardiotocography cases (RR 0.88, 95% CI 0.45–1.75),[10] and in subgroup analysis of trials which used the four-tier system for the ST waveform an analysis arm (RR 0.79, 95% CI 0.61–1.03).[7,9–11]

DISCUSSION

This meta-analysis from six high-quality and carefully conducted RCTs, including more than 26,000 singleton gestations, evaluating the effectiveness of standard cardiotocography alone and with additional ST waveform analysis during labor, showed that ST waveform analysis+cardiotocography did not improve perinatal outcomes compared with cardiotocography alone. Pooled results showed a positive effect of ST waveform analysis on reducing the need for operative vaginal delivery (either forceps or vacuum) and fetal blood sampling, a procedure rarely performed in the United States and itself of unproved value.[18] Although statistically significant, the clinical effect of a 9% decrease in operative vaginal delivery is unclear. Furthermore, in the largest trial, the U.S. study of Belfort et al, rates of operative vaginal delivery were 5.9% with and without ST waveform analysis.[12]

Our meta-analysis included appropriately powered, large-scale, well-designed high-quality RCTs. Test of heterogeneity and sensitivity analyses all point to the noneffectiveness of ST waveform analysis. Our findings showed that ST waveform analysis during labor as an adjunct to cardiotocography did not improve perinatal outcomes either in trials in which continuous cardiotocography was routinely used or in trials in which continuous cardiotocography was used only in case of high-risk pregnancy. Our results are therefore broadly generalizable.

Six other reviews have evaluated the efficacy of ST waveform analysis+cardiotocography compared with cardiotocography alone.[19–24] However, these prior meta-analyses did not include all currently available RCTs, in particular the latest and largest one,[12] and therefore had a smaller number of randomized women included.

Our study has several strengths. This meta-analysis included all studies published so far on the topic, studies of high quality and with a low risk of bias according to the Cochrane risk of bias tools. The number of randomized women was very high. To our knowledge, no prior meta-analysis on this issue is as large, up-to-date, or comprehensive. We assessed the primary

Perinatal Death	Neonatal Encephalopathy	Meconium Aspiration Syndrome	Shoulder Dystocia	Fetal Blood Sampling
2/1,219 (0.2) vs 0/1,215	1/1,219 (0.1) vs 4/1,215 (0.3)	N/R	N/R	93/1,219 (7.6) vs 114/1,215 (9.4)
3/2,519 (0.1) vs 2/2,447 (0.1)	0/2,519 vs 6/2,447 (0.3)	N/R	N/R	234/2,519 (9.3) vs 261/2,447 (10.7)
0/714 vs 0/722	0/714 vs 1/722 (0.1)	N/R	N/R	51/733 (7.0) vs 115/739 (15.6)
0/399 vs 1/400 (0.3)	1/399 (0.3) vs 1/400 (0.3)	N/R	N/R	108/399 (27.0) vs 248/400 (62.0)
3/2,827 (0.1) vs 2/2,840 (0.1)	3/2,827 (0.1) vs 1/2,840 (0.1)	N/R	N/R	301/2,827 (10.6) vs 578/2,840 (20.4)
3/5,532 (0.1) vs 1/5,576 (0.1)	4/5,532 (0.1) vs 5/5,576 (0.1)	20/5,532 (0.4) vs 20/5,576 (0.3)	140/5,532 (2.5) vs 158/5,576 (2.8)	N/P
11/13,210 (0.1) vs 6/13,200 (0.1)	9/13,210 (0.1) vs 18/13,200 (0.2)	20/5,532 (0.4) vs 20/5,576 (0.3)	140/5,532 (2.5) vs 158/5,576 (2.8)	787/9,483 (8.3) vs 1,316/7,641 (17.2)
0	4	N/A	N/A	91
M-H, fixed	M-H, fixed	M-H, fixed	M-H, fixed	M-H, Random
1.71 (0.67–4.33)	0.62 (0.25–1.52)	1.01 (0.54–1.87)	0.90 (0.72–1.13)	**0.59 (0.45–0.79)**

Table 4. Mode of Delivery

Reference	OVD	Cesarean Delivery	Operative Delivery*
Westgate et al,[8] 1993	229/1,219 (18.8) vs 262/1,215 (21.6)	176/1,219 (14.4) vs 232/1,215 (19.1)	405/1,219 (33.2) vs 494/1,215 (40.7)
Amer-Wahlin et al,[7] 2001	244/2,519 (9.7) vs 278/2,447 (11.4)	210/2,519 (8.3) vs 222/2,447 (9.1)	454/2,519 (18.1) vs 500/2,447 (20.4)
Ojala et al,[9] 2006	70/733 (9.5) vs 79/739 (10.7)	47/733 (6.4) vs 35/739 (4.7)	117/733 (16.0) vs 114/739 (15.4)
Vayssiere et al,[10] 2007	80/399 (20.0) vs 83/400 (20.1)	54/399 (13.5) vs 65/400 (16.3)	134/399 (33.6) vs 148/400 (37.0)
Westerhuis et al,[11] 2010	384/2,827 (13.6) vs 431/2,840 (15.2)	405/2,827 (14.3) vs 391/2,840 (13.8)	789/2,827 (27.9) vs 822/2,840 (28.9)
Belfort et al,[12] 2015	329/5,532 (5.9) vs 328/5,576 (5.9)	934/5,532 (16.9) vs 910/5,576 (16.3)	1,263/5,532 (22.8) vs 1,238/5,576 (22.2)
Total	1,336/13,229 (10.1) vs 1,461/13,217 (11.1)	1,826/13,229 (13.8) vs 1,855/13,217 (14.0)	3,162/13,229 (23.9) vs 3,316/13,217 (25.1)
I^2 (%)	0	65	68
Method used	M-H, fixed	M-H, random	M-H, random
RR (95% CI)	**0.91 (0.85–0.98)**	0.96 (0.85–1.08)	0.93 (0.86–1.01)

OVD, operative vaginal delivery (either forceps or vacuum); M-H, Mantel-Haenszel test; RR, relative risk; CI, confidence interval.
Data are n ST waveform analysis group vs n cardiotocography-only group with percentage.
Bold indicates statistical significance.
* Either cesarean delivery or OVD.

outcome in several sensitivity analyses to reduce the clinical heterogeneity between the trials (eg, inclusion criteria). The statistical heterogeneity within the studies in the primary outcome and in most of the secondary outcomes was low (I^2 less than 50%).

Limitations of our study are inherent to the limitations of the included RCTs. Only one trial was double-blind. Although four authors kindly provided unpublished data from their trials, we did not have access to all the original databases and so individual patient-level meta-analysis was not feasible. Neonatal encephalopathy was not uniformly defined: two RCTs defined this outcome using the same diagnostic criteria (ie, Sarnat and Sarnat criteria stage 1–3)[25]; the American trial used the new criteria by Shankaran et al.[26] Base deficit was usually calculated in the extracellular fluid compartment using the Siggaard-Andersen algorithm, whereas the Finnish RCT reported only data regarding blood base deficit. We could not obtain data regarding composite perinatal outcome (ie, primary outcome) and regarding incidence of metabolic acidosis from Westgate et al.[8] The American RCT, which is the largest trial, had an incidence of metabolic acidosis lower than the other RCTs possibly resulting from the higher number of low risk pregnancies included[12]; this issue raises the question of the methodologic differences between the included studies. Indeed, most trials included only women with either abnormal cardiotocography or meconium,[10] or only high-risk pregnancies,[7,8,11] so women at higher risk for abnormal perinatal outcome and neonatal metabolic acidosis (Table 1). Instead, the two other trials[9,12] did not select for this higher risk population and therefore included lower risk pregnancies.

In conclusion, our findings provide high-quality evidence that use of ST waveform analysis during labor as an adjunct to the standard electronic fetal monitoring does not improve perinatal outcomes or decrease cesarean delivery rates.

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